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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/658,165	09/09/2003	Randal Lee Schapaugh	00550.US1	5705

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PHARMACIA & UPJOHN
7000 Portage Road
KZO-300-104
KALAMAZOO, MI 49001

EXAMINER	
WALLENHORST, MAUREEN	
ART UNIT	PAPER NUMBER
1743	

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
3 MONTHS	03/06/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Office Action Summary	Application No.	Applicant(s)	
	10/658,165	SCHAPAUGH ET AL.	
	Examiner	Art Unit	
	Maureen M. Wallenhorst	1743	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-38 (renumbered)* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-38* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *3/11/04, 6/14/04*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

1. Applicants are notified that the claims have been renumbered as 1-38 since the original claims were misnumbered as 1-22 and 24-39.

2. Claims 9, 21-22 and 34 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

On line 1 of claim 9, the phrase "selected from" should be changed to –selected from the group consisting of—so as to use proper Markush language. This same change should also be made on lines 1-2 of claim 34. On line 2 of claim 9, the square symbols should be deleted. On line 2 of claim 9, the phrase "adrenergic agonists" has been repeated twice. In addition, on lines 2-3 of claim 9, the phrase "adrenergic blockers" has been repeated twice. Both recitations of adrenergic blockers are understood to be beta blockers, and thus, are the same.

In claims 21-22, the phrase "optimal pH" is indefinite since it is not clear what constitutes "optimal". In addition, what does the pH have to be optimal for?

3. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

4. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection

is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

5. Claims 1-3, 5-25, 27 and 32-35 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-2, 5-11, 13-17, 19, 21-24, 27, 29-30 and 35 of copending Application No. 10/658,164. Although the conflicting claims are not identical, they are not patentably distinct from each other because both sets of claims recite a method of characterizing the transfer of an analyte from a non-aqueous liquid composition to an aqueous medium comprising the steps of providing a non-aqueous liquid composition comprising an analyte and a non-aqueous base, combining the non-aqueous liquid composition with an aqueous dissolution medium, agitating and mixing the non-aqueous liquid composition and the aqueous dissolution medium and determining the amount of analyte in the aqueous dissolution medium at multiple time points after the combining and agitating steps. The claims of U.S. application serial no. 10/658,164 fail to recite that an emulsion forms upon agitating and mixing the non-aqueous liquid composition and the aqueous dissolution medium. However, it would have been obvious to one of ordinary skill in the art at the time of the instant invention to realize that an emulsion inherently forms as a result of the contact and agitation

between the aqueous dissolution medium and the non-aqueous liquid composition recited in the claims of U.S. application serial no. 10/658,164 since the method recited in the claims of application serial no. 10/658,164 combines an oil such as cottonseed oil as a non-aqueous liquid base with an analyte such as ceftiofur, which are the same types of non-aqueous base and analyte as recited in the instant claims, and then combines this non-aqueous liquid composition with an aqueous dissolution medium, which is also the same step as recited in the instant claims. Therefore, one of ordinary skill in the art would expect that an emulsion would form between the non-aqueous liquid composition and the aqueous dissolution medium in the method recited in the claims of U.S. application serial no. 10/658,164 since the same type of reagents are being combined under the same conditions (i.e. agitation) as in the claims of the instant invention, and an emulsion inherently forms between two different dispersed phases (i.e. an oil and an aqueous liquid) when the phases are immiscible liquids.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

6. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

7. Claims 1-2, 5-18, 22-23, 25 and 32-38 are rejected under 35 U.S.C. 102(b) as being anticipated by Dunn et al (US Patent no. 5,721,359, submitted in the Information Disclosure Statement (IDS) filed on March 11, 2004).

Dunn et al teach of a non-aqueous liquid composition containing a non-aqueous base and an analyte. The non-aqueous base is an oil such as corn oil, peanut oil, sesame oil, olive oil, safflower oil, soybean oil, cottonseed oil, rapeseed oil and mixtures thereof. Preferably, the non-aqueous base is cottonseed oil. The analyte is a cephalosporin antibiotic material known as ceftiofur. The non-aqueous liquid composition is used as a pharmaceutical composition in a sustained release dosage form. The pharmaceutical composition can also contain excipients such as dispersing agents, emulsifying agents, buffers, sweeteners, flavoring agents, colorants and preservative agents. See lines 10-39 in column 3 and lines 21-31 in column 9 of Dunn et al. In example 4 of Dunn et al, a sustained release oil formulation containing ceftiofur free acid and cottonseed oil is taught. In example 7 of Dunn et al, an in vitro dissolution test of the ceftiofur oil suspension formulation is disclosed in order to characterize the in vivo performance of this pharmaceutical composition for public use. In the dissolution test, samples of the non-aqueous liquid oil composition containing ceftiofur antibiotic are loaded into a dissolution apparatus containing an aqueous dissolution medium at an optimal pH of 7. The non-aqueous liquid composition and the aqueous dissolution medium are agitated with a rotating paddle, and at different time points after being combined together, samples of the aqueous dissolution medium are taken and tested for the amount of ceftiofur analyte therein. See Figure 6 in Dunn et al that plots the amount of ceftiofur analyte released into the aqueous dissolution medium as a function of time. The mixing and agitating of the non-aqueous liquid composition having ceftiofur antibiotic therein with the aqueous dissolution medium in the dissolution apparatus inherently forms an emulsion, at least at the surface of the aqueous dissolution medium, since an emulsion

forms between two different immiscible liquids (i.e. an oil and an aqueous liquid) to some extent when dispersed and mixed with one another.

8. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

9. The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

10. Claims 3-4, 19-21, 24 and 26-31 are rejected under 35 U.S.C. 103(a) as being unpatentable over Dunn et al in view of Conti et al (article submitted in the IDS filed on March 11, 2004). For a teaching of Dunn et al, see previous paragraphs in this Office action. Dunn et al fail to teach that the samples of aqueous dissolution medium taken from the dissolution apparatus at different time points after combining the non-aqueous liquid composition with the aqueous dissolution medium are filtered first before being tested, fail to teach that the aqueous dissolution medium contains a buffer, fail to teach that the aqueous dissolution medium can contain a surfactant, and fail to teach that the dissolution apparatus is a reciprocating shaker.

Conti et al teach of in vitro dissolution tests for different drug delivery systems. Four different types of dissolution methods and apparatuses are evaluated including a paddle stirring

apparatus, a rotating bottle apparatus, a shaker incubator and a recycling flow through cell. In each of these devices, the aqueous dissolution medium used is an aqueous phosphate buffered solution at an optimal pH of 7.4. In some of the tests performed, the surfactant Polysorbate 20 is added to the aqueous dissolution medium. In each of the dissolution tests, samples of the aqueous dissolution medium are taken at different time points after being admixed with a drug formulation, then are filtered through a Millipore membrane having 0.22 micron pores, and analyzed by UV spectrophotometry. See pages 1224-1226 in Conti et al. Conti et al teach that the presence of a surfactant in the aqueous dissolution medium doubles the amount of drug released into the dissolution medium for all of the methods tested. Faster drug release is also found for the aqueous dissolution medium containing a phosphate buffer at pH 7.4 and at a high ionic strength.

Based upon the combination of Dunn et al and Conti et al, it would have been obvious to one of ordinary skill in the art at the time of the instant invention to filter the samples of aqueous dissolution medium taken from the dissolution apparatus taught by Dunn et al before being analyzed for ceftiofur concentration since Conti et al disclose that filtering aqueous dissolution media before analysis is advantageous in order to remove any excipient material that may interfere with the analysis, thereby producing more accurate results. It also would have been obvious to one of ordinary skill in the art to use a phosphate buffered aqueous solution as the aqueous dissolution medium in the dissolution method taught by Dunn et al since Conti et al disclose that such a phosphate buffered dissolution medium serves to produce faster drug release from a drug formulation into the aqueous medium. It also would have been obvious to one of ordinary skill in the art to add a surfactant to the aqueous dissolution medium taught by Dunn et

al since Conti et al disclose that a surfactant in an aqueous dissolution medium also helps to increase the amount of drug that is released into the dissolution medium during a dissolution test. It would have been obvious to one of ordinary skill in the art at the time of the instant invention to use a reciprocating shaker as the dissolution test apparatus for performing the dissolution test taught by Dunn et al rather than a paddle apparatus, since Conti et al teach that a shaker device is an equivalent dissolution test apparatus to a paddle device, and both provide the required agitation motion to a mixture of a drug formulation and an aqueous dissolution medium to cause the release of the drug into the dissolution medium. With regards to instant claim 27, it would have been obvious to one of ordinary skill in the art to vary the ratio of the non-aqueous liquid composition to the aqueous dissolution medium taught by Dunn et al to the levels recited since the amount of materials used in a method is a result effective variable that can be experimentally varied in order to optimize a particular procedure being performed with the materials.

11. The prior art made of record and not relied upon is considered pertinent to applicant's disclosure.

Please make note of: Qureshi, Hutchins et al, Muller, Fassihi, Benz, Smolen, Goodhart et al and Kirschner et al who all teach of devices for performing dissolution tests on pharmaceutical compositions.

12. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Maureen M. Wallenhorst whose telephone number is 571-272-1266. The examiner can normally be reached on Monday-Thursday from 6:00 AM to 4:30 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jill Warden, can be reached on 571-272-1267. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Maureen M. Wallenhorst
Primary Examiner
Art Unit 1743

mmw

February 28, 2007

Maureen M. Wallenhorst
MAUREEN M. WALLENHORST
PRIMARY EXAMINER
GROUP [redacted] 1700